ABSTRACT

"Labeling reagents, methods for the synthesis of such reagents and methods for the detection of biological molecules" - <u>BIOMERIEUX S.A.</u>

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The present invention relates to a temperature-stable labeling reagent of formula (0):

$$R^2$$
— $(Z-(CH_2)_p)_m$ — $(L)_n$ — Y — X
 R^4
 $(A)_u$
 R^1

in which:

- R¹ represents H or an alkyl, aryl or substituted aryl group,
- R² represents a detectable marker or at least two detectable markers interlinked by at least one multimeric structure.
 - L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,
 - R³ and R⁴ represent, independently of one another: H, NO₂, Cl, Br, F, I, R² -(L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,
 - A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and u is an integer between 0 and 2, preferably 0 or 1,
- -Y-X- represents -CONH-, -NHCO-, -CH₂O-, -CH₂S-,
 - -Z- represents -NH-, -NHCO-, -CONH- or -O-,
 - m is an integer between 1 and 10, preferably between 1 and 3, and
 - p is an integer between 1 and 10, preferably between 1 and 3.
- The present invention also describes a method for the synthesis of said labels and also applications for the labeling of biological molecules, in particular of nucleic acids, with a labeling reagent bearing the diazomethyl function.

The invention is particularly suitable for use in the field of diagnostics.